Guidelines for reporting domestic suspect and confirmed human cases of avian influenza A(H5) to CDC and the collection and shipping of specimens for influenza A(H5) testing

Since February 3, 2004, CDC has issued several Health Alert updates requesting that local and state health departments enhance surveillance for human avian influenza A (H5) illnesses. The following document contains more detailed information on reporting and on the collection, shipping and testing of clinical specimens. A case report form and instructions are also attached.

In collaboration with state and local health departments, CDC is collecting information on suspect and confirmed human influenza A(H5) cases in the United States. This effort is intended to enhance current influenza surveillance for early identification of patients with influenza A(H5) infection. CDC requests that state and local health departments obtain specimens for influenza virus testing on patients meeting the influenza A (H5) surveillance criteria below.

Influenza A (H5) Surveillance Criteria

1. Patient is hospitalized and has:
    a. radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established **and;**
    b. a history of travel within 10 days of symptom onset to a country with documented H5N1 avian influenza infections in poultry or humans. Ongoing listings of Asian countries affected by avian influenza are available from the World Organization for Animal Health (http://www.oie.int/downld/AVIAN INFLUENZA/A_AI-Asia.htm).

OR

2. Patient is hospitalized or ambulatory and has:
    a. documented temperature of >100.4°F (>38°C), **and**;
    b. cough, sore throat, or shortness of breath; **and either;**
    c. history of contact within 10 days prior to onset of symptoms with:
        i. poultry or domestic birds (e.g., visited a poultry farm, a household raising poultry, or a bird market) in an affected country **or**
        ii. a patient with known or suspected influenza A(H5) infection.

Patients meeting the influenza A (H5) surveillance criteria may be tested at the state/local level for influenza A or influenza A(H5) if laboratory capacity is available. **See Laboratory Testing Procedures section below for precautions on working with clinical specimens that potentially contain influenza A(H5).**

Specimens from persons meeting the influenza A (H5) surveillance criteria should be sent to the CDC if:

1. specific influenza A(H5) testing done at the state /local laboratory is positive **(this should be done only if the laboratory is able to test for influenza A(H5) by PCR or if they have a BSL 3 with enhancements facility for influenza A(H5) viral culture)**,

OR

2. testing for influenza A is positive by PRC or rapid antigen detection* and the referring jurisdiction is not equipped to test for influenza A(H5),

OR

3. the referring jurisdiction is not equipped to test for influenza A by PCR and is requesting testing at CDC.

State and local health departments **should not** report patients who meet the clinical and epidemiologic criteria but who have an alternative laboratory confirmed diagnosis (e.g. influenza A(H3), influenza A(H1), influenza B, or a non-influenza etiology) or who have tested negative for influenza A by PCR.

*Because the sensitivity of commercially available rapid diagnostic tests for influenza may not always be optimal, CDC also will accept specimens from persons meeting the above clinical criteria even if they test negative by influenza rapid diagnostic testing if PCR assays are not available at the state laboratory.

A **confirmed human influenza A(H5) case** is a case meeting surveillance criteria above that is laboratory confirmed by CDC as influenza A(H5) positive by:

a. PCR, or
b. viral culture, or
c. influenza A(H5) specific serology

HIPAA

CDC is conducting these activities in its capacity as a public health authority, as defined by the Health Insurance Portability and Accountability Act (HIPAA). Health care providers and health departments **may therefore disclose protected health information to CDC** without individual authorization. The information being requested represents the minimum necessary to carry out the public health purposes of this project pursuant to 45 CFR §164.514(d) of the Privacy Rule, and protected health

information will not be disseminated. Nevertheless, individual local and state health department privacy policies may vary, and should be followed accordingly.

Reporting Suspect Cases of Human Influenza A(H5)

A. Initial Report: Prior to submitting a case report form, health department officials should first contact the CDC Director's Emergency Operations Center (DEOC) at 770-488-7100. This number is available 24 hours a day, 7 days a week. DEOC staff will notify a member of the human influenza A(H5) surveillance team who will contact the health department and provide a unique CDC case ID number for each case which meets the surveillance criteria.

B. Written Materials

1. **Case Report Form:** Following the initial telephone report, health department officials should submit a completed CDC case report form. This form is available through Epi-X, or by contacting CDC DEOC at 770-488-7100.
2. **Sending case report form to CDC:** Materials should be faxed to CDC at 888-232-1322. Please include the CDC case ID number, contact information, and a cover sheet with the header "ATTN: Influenza A(H5N1) case reporting." Rapid return of information is of high priority; complete as much of the case report form as possible and transmit to CDC within 3 to 5 business days of first contact. The remaining information can be sent as soon as it is available. CDC staff will assist local and state health departments in completing the case report forms as needed.

C. Laboratory Procedures, Specimen Collection and Shipment

1. **Laboratory precautions for influenza A (H5) testing:** Highly pathogenic avian influenza A(H5N1) is classified as a select agent and **must be** worked with under Biosafety Level (BSL) 3+ laboratory conditions.
    a. **Culture only at BSL 3 with enhancements level facilities.** This includes controlled access double door entry with change room and shower, use of respirators, decontamination of all wastes, and showering out of all personnel. Laboratories working on these viruses must be certified by the U.S. Department of Agriculture. CDC does **not recommend** that virus isolation studies on respiratory specimens from patients who meet the above criteria be conducted unless stringent BSL 3 with enhancements conditions can be met and work is separate from other human influenza A (i.e., H1 or H3) virus work. Therefore, respiratory virus cultures should not be performed in most clinical laboratories and cultures should not be ordered for patients suspected of having influenza A (H5N1) infection.

b. **PCR and rapid antigen detection:** Clinical specimens from suspect influenza A(H5) cases may be tested at the state/local public health laboratory by PCR assays using standard BSL 2 work practices in a Class II biological safety cabinet. In addition, commercial rapid antigen detection testing can be conducted under BSL 2 levels to test for influenza.

2. To assist public health public health laboratories respiratory illness diagnostic efforts, CDC has developed real-time PCR protocols for a number of respiratory pathogens, including influenza A and B viruses, adenovirus, metapneumovirus, Legionella, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*. **These protocols are currently available only to public health laboratories and have been posted at the APHL Members Only (password required) Web site** www.aphl.org/Members_Only/index.cfm, under SARS. These protocols are not available in all public health laboratories, and physicians should consult with their local public health laboratory when ordering these tests.

3. **Sample Collection and Shipping instructions**
   a. **Respiratory specimens:** Aliquots of extracted RNA (for PCR positives) and/or clinical specimen (i.e., nasopharyngeal and oropharyngeal swabs, nasal washings, tracheal aspirates) should be sent through established channels (e.g., via the state laboratory) or directly to CDC for viral characterization.

      Specimens should be frozen at -70^{o} C and shipped on **dry ice** directly to CDC **overnight** to the address in Section 4d.

   b. **Serum specimens:** A serum sample (5-10 cc) should be collected in a serum separator tube, centrifuged, and stored locally at -20^{o} F. A convalescent serum sample should be drawn 2-4 weeks later and both acute and convalescent sera should be sent to the CDC for serologic testing.

   c. **Autopsy Specimens:** CDC can perform immunohistochemical (IHC) staining for influenza A(H5) viruses on autopsy specimens. Viral antigens may be focal and sparsely distributed in patients with influenza, and are most frequently detected in respiratory epithelium of large airways. Larger airways (*particularly primary and segmental bronchi*) have the highest yield for detection of influenza viruses by IHC staining. Collection of the appropriate tissues ensures the best chance of detecting the virus by (IHC) stains. If influenza is suspected, a minimum total of 8 blocks or fixed tissue specimens representing samples from each of the following sites should be obtained and submitted for evaluation:

1. Central (hilar) lung with segmental bronchi
2. Right and left primary bronchi
3. Trachea (proximal and distal)
4. Representative pulmonary parenchyma from right and left lung

In addition, representative tissues from major organs should be submitted for evaluation. In particular, for patients with suspected myocarditis or encephalitis, specimens should include myocardium (right and left ventricle) and CNS (cerebral cortex, basal ganglia, pons, medulla, and cerebellum). Specimens should be included from any other organ showing significant gross or microscopic pathology.

Specimens may be submitted as:

1. Fixed, unprocessed tissue in 10% neutral buffered formalin, or
2. Tissue blocks containing formalin-fixed, paraffin-embedded specimens, or
3. Unstained sections cut at 3 microns placed on charged glass slides (10 slides per specimens)

Specimens should be sent at room temperature (**NOT FROZEN**)

Please include a copy of the autopsy report (preliminary or final if available), and a cover letter outlining a brief clinical history and the full name, title, complete mailing address, phone, and fax numbers of the submitter, in the event that CDC pathologists require further information. Referring pathologists may direct specific questions to CDC pathologists.

4. Shipping Instructions:

a. Specimens should be submitted to CDC by state and local health departments. The Influenza A(H5) Epi/Surveillance Team should be contacted at 770-488-7100 before sending specimens for influenza A(H5) testing.

b. When sending clinical specimens, please include the **specimen inventory sheet (appendix A)**, include the assigned **CDC case ID number,** and indicate **"Human Influenza A(H5) surveillance"** on all materials and specimens sent.

c. Please include the **CDC case ID number** on all materials forwarded to CDC. Protocols for standard interstate shipment of etiologic agents should be followed, and are available at http://www.cdc.gov/od/ohs/biosfty/shipregs.htm.

d. Address for respiratory and serum specimens:

Dr. Alexander Klimov, PhD, ScD, Chief
Strain Surveillance Section
Influenza Branch, CDC
c/o DASH
1600 Clifton Road
Atlanta, GA 30333
Phone: 404-639-3387 or 3591, fax: 404-639-2334, email: AKlimov@cdc.gov

Address for autopsy specimens

Dr. Sherif Zaki, MD, PhD
Infectious Disease Pathology Activity
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control and Prevention
Mailstop G-32, Bldg 1, Rm 2301
1600 Clifton Road
Atlanta, GA 30333
Phone: 404-639-3133
fax: 404-639-3043
email: SZaki@cdc.gov

5. ADDITIONAL INFORMATION

Any questions regarding reporting procedures or specimen shipment can be directed to the influenza special investigations team:

Influenza A(H5N1) Epi/Surveillance Team
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control and Prevention
Mailstop A-32, Bldg 6, Rm 122
1600 Clifton Road
Atlanta, GA 30333
Phone: 770-488-7100, Fax: 888-232-1322
Email: eocinfluenza@cdc.gov

PHONE NUMBERS

Reporting cases and Notification of specimen shipments	770-488-7100
Fax number for case report forms	888-232-1322
Requests for specimen testing	770-488-7100
Dr. Alexander Klimov, Strain Surveillance	404-639-3387
Dr. Sherif Zaki, Infectious Disease Pathology	404-639-3133

Appendix A

CDC CASE ID:

List specimens sent to the CDC		
Select a SOURCE* from the following list for each specimen: Serum (acute), serum (convalescent), NP swab, NP aspirate, broncheoalveolar lavage specimen (BAL), OP swab, tracheal aspirate, or tissue		
Specimen Type #1: □ Clinical Material □ Extracted RNA □ Virus Isolate	Source*: _____	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen Type #2: □ Clinical Material □ Extracted RNA □ Virus Isolate	Source*: _____	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen Type #3: □ Clinical Material □ Extracted RNA □ Virus Isolate	Source*: _____	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen Type #4: □ Clinical Material □ Extracted RNA □ Virus Isolate	Source*: _____	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen Type #5: □ Clinical Material □ Extracted RNA □ Virus Isolate	Source*: _____	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Carrier:	Tracking #:	